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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,581	02/11/2004	David L. Klein	GR8003 US	6020

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EXAMINER	
RAMDHANIE, BOBBY	
ART UNIT	**PAPER NUMBER**
1797	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,581	KLEIN ET AL.	
	Examiner	Art Unit	
	Bobby Ramdhanie, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-31 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10-31 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 1-8, 10-14, 19, 20, 22, 23, and 25-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Rao (US 2002/0025547 A1). Regarding Claim 1, Rao teaches a well plate comprising a plurality of wells, each well being defined by at least one surface that defines a cavity having an opening, wherein each well comprises at least one aperture through the at least one surface of the well, the aperture configured to provide a gas supply access to the interior of the well; and at least one of a pH level sensor and dissolved oxygen sensor disposed within the well (Figures 1 and 2).

3. For Claim 2, Rao teaches the well plate of Claim 1 wherein each well is defined by a bottom surface and at least one side surface that defines the opening m the at least one aperture is through the bottom surface (Figure 6). Examiner takes the position that an window can also define an aperture (Figure 6 and [0097]).

4. For Claim 3, Rao teaches the well plate of Claim 1 wherein the at least one of a pH level sensor and a dissolved oxygen sensor (Figure 1) comprises a fluorescent material ([0096]) disposed on the interior of that at least one surface of the well.

5. For Claim 4, Rao teaches the well plate of Claim 3 wherein the at least one of a pH level sensor and a dissolved oxygen sensor are disposed on the interior of the bottom surface of the well (Figure 6).

6. For Claim 5, Rao teaches the well plate of Claim 1, wherein at least one of a pH level sensor and a dissolved oxygen sensor comprise at least one probe that is coupled to the interior of the well (Figure 3b, [0096]).

7. For Claim 6, Rao teaches the well plate of Claim 5, further comprising a lid configured to be placed over the plurality of wells, wherein the at least one probe extends from the lid into the interior of the well (Figure 2).

8. For Claim 7, Rao teaches the well plate of Claim 1, further comprising at least one membrane coupled to the at least one surface of each well and covering the at least one aperture, wherein the membrane is formed from a gas permeable material and the gas is supplied through the membrane (Figure 6, [0097]).

9. For Claim 8, Rao teaches the well plate of Claim 7 wherein each well is defined by a bottom surface, the at least one aperture is through the bottom surface, and at least one side surface and the at least one membrane is coupled to the bottom surface of each well ([0097] and Figure 6).

10. For Claim 10, Rao teaches the well plate of Claim 7 wherein the membrane is formed from porous material with pores less than 0.2 μm ([0057]).

11. For Claim 11, Rao teaches the well plate of Claim 7 wherein a plurality of membranes is used with each well. (Figure 6).

12. For Claim 12, Rao teaches the well plate of Claim 1 wherein each well comprises a plurality of apertures through the at least one surface of the well, the plurality of apertures configured to provide a gas supply to the interior of the well (Figure 2).

13. For Claim 13, Rao teaches the well plate of Claim 1 wherein each well comprises an array of apertures through the at least one surface of the well, the array the plurality of apertures configured to provide a gas supply to the interior of the well, wherein each aperture in the array is approximately 0.2 mm to 1 mm in diameter (Figure 2, and [0127]).

14. For Claim 14, Rao teaches the well plate of Claim 1, wherein each well further comprises a second aperture through the at least one surface of the well, the second aperture configured to place a temperature control element in thermal contact with the interior of the well, and a third aperture through the at least one surface of the well, the third aperture configured to place a temperature measurement element in thermal contact with the interior of the well ([0068], [0012], [0112], [0113], [0115]).

15. For Claim 19, Rao teaches a well plate comprising a plurality of wells ([0068], [0012]), each having at least one surface that defines an opening at the top of the well, wherein each well comprises a first aperture through the at least one surface of the well, the first aperture configured to provide a gas supply ([0127]) access to the interior of the well, and at least one additional aperture through the at least one surface of the well, the at least one additional aperture through the at least one additional aperture configured ([0011-0012]) to place one of a temperature control element ([0113]) and a

temperature measurement element ([0115]) in thermal contact with the interior of the well.

16. For Claim 20, Rao teaches the well plate of Claim 19 ([0068], [0012], [0127]) wherein the at least one additional aperture through the at least one surface of the well comprising with the second aperture through one of the surfaces of the well, second aperture configured to place a temperature measurement element in thermal contact with the interior of the well ([0013]), and a third aperture through one of the surfaces of the well the third aperture configured to place a temperature control element in thermal contact with the interior of the well ([0115]). Figure 6 shows the well with a pH and oxygen sensor chemical films on the bottom of the well. Rao also teaches that the temperature sensor can be a film and placed on the bottom of the well. All three of these films sit on top of an aperture of the well.

17. For Claim 22, Rao teaches the well plate according to Claim 19, wherein the first aperture is one of a plurality of apertures through at least one surface of the well that are configured to provide a gas supply access to the interior of the well (Figure 2, [0011-0012], [0013], and [0015]).

18. For Claim 23, Rao teaches the well plate of Claim 22, wherein the plurality of apertures form an array of apertures, wherein each aperture in the array is approximately 0.2 to 1 mm in diameter (Figure 2, [0127]). Examiner takes the position that 0.25 mm is within the specified 0.2 – 1 mm diameter range.

19. For Claim 25, Rao teaches the well plate in Claim 19. Rao also teaches the means for sensing at least one of the pH level and dissolved oxygen within the well ([0106]).

20. For Claim 26, Rao teaches the well plate of 25, wherein the means for sensing comprises one or more fluorescent materials disposed on the bottom interior surface of the well (Figure 6, [0096]).

21. For Claim 27, Rao teaches the well plate of Claim 25, wherein the means for sensing comprises at least one probe that extends into the interior of each well ([0104]).

22. For Claim 28, Rao teaches the well plate of Claim 27. Rao also teaches the well plate further comprising a lid configured to be placed over the wells wherein, the at least one probe extends from the lid into the interior of the well (Figure 8).

23. For Claim 29, Rao teaches the well plate of Claim 19, further comprising at least one membrane coupled to the at least one surface of each well and covering the at least the first aperture wherein the membrane is formed from a gas permeable material and the gas is supplied through the membrane (Figure 2 and [0057]).

24. For Claim 30, Rao teaches the well plate of Claim 29, wherein the at least one membrane is a first membrane coupled to the at least one surface of each well and covering the first aperture (Figure 2, [0057]), the well plate further comprising a second membrane coupled to the at least one surface of each well and covering the at least one additional aperture (Figure 2 [0057]).

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

27. Claims 15-17, 21, 24, 31, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao (US 2002/0025547 A1) in further in view of Olivier (US 2003/0219360 A1). Regarding Claim 15, Rao teaches the well plate of Claim 1 wherein at least one surface of each well has a first thickness (Figure 1, [0029]). Rao however, does not teach the indentation having a second thickness that is less than the first thickness. Olivier teaches a well plate having an indentation having a second thickness that is less than the first thickness (Figure 7). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Rao with Olivier because the design of the microtiter plate in Olivier would allow for the microtiter plate to be in SBS format and allow for a multistack bioreactor to be created ([0017]).

28. For Claim 16, Rao teaches the use of a well plate in accord with Claim 15. Rao does not teach a well plate having an indentation with a second thickness. Olivier teaches a well plate with the second thickness (Figure 7) which further comprises a thermally conductive material (Olivier, [0020]) within the indentation. It would have been obvious to one skilled in the ordinary art at the time the invention was made to modify Rao with Olivier because the thermally conductive material would allow for more efficient thermal energy transfer between bioreactor and the bioreactor platform (Rao, [0120]).

29. For Claim 17, Rao teaches all of the claim limitations according to Claim 14. Rao further teaches a first membrane coupled to at least one surface of each well (Figure 3b) and covering the at least one aperture and a second membrane coupled to the at least one surface of each well and covering at least one of the second and third apertures (Figure 2). Rao however, does not teach the indentations on the surface of the well to provide a different thickness. Olivier teaches this feature (Figure 7). It would have been obvious to one skilled in the ordinary art to modify Rao with Olivier because the well plate in Olivier is commonly available as a standard plate and is made in compliance with SBS format.

30. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rao (US 2002/0025547 A1). Regarding Claim 18, Rao teaches all of the claim limitations according to Claim 14. Rao further teaches a membrane coupled to the at least one surface of each well and covering the at least one aperture and the second and third apertures [0057], the membrane having a first thickness over the at least one aperture

and having a second thickness over the second and third apertures, the second thickness being greater than the first thickness [0096 & 0097]. Rao does not explicitly teach that these membranes have varies thicknesses. It would have been obvious to one of ordinary skill in the art to modify Rao so that the membranes have varied thicknesses because this would prevent cells from giving false positive signals to the detectors that lie underneath the membranes and only allow chemicals and gases to interact with the chemicals inside the sensors.

31. For Claim 21, Rao teaches the well plate of Claim 19. Rao does not teach at least one additional aperture through a bottom surface of each well. Olivier teaches a well plate that possesses the at least one additional aperture through a bottom surface of each well (Figure 7). It would have been obvious to one skilled in the ordinary art to modify Rao in view of Olivier because the drain at the bottom of each well would allow fluid in the well to escape and drain into a collection plate ([0025]).

32. For Claim 24, Rao teaches the well plate in Claim 19. Rao does not teach the well plate wherein the first aperture comprises a plurality of supporting ribs extending across the first aperture. Olivier teaches a plurality of support ribs extending across the first aperture (Figure 6). It would have been obvious to modify Rao in view of Olivier because the design of Olivier would allow for structural support upon use of a vacuum to remove liquid from the well.

33. For Claim 62, Rao teaches all of the claim limitations according to Claim 1. Rao does not teach that each well has a bottom and the at least one aperture is through the bottom. Olivier teaches this feature (Figure 7 Item number 33).

34. Claims 18 & 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao (US 2002/0025547 A1) and in further in view of Olivier (US 2003/0219360 A1), Rao (Rao, 1994), and Wolfbeis (Wolfbeis, 1995). Regarding Claim 18, Rao teaches the well plate of Claim 14 wherein at least one surface of each well has a first thickness ([0029]), the well plate of Claim 14 containing the two sensors of Rao et al, 1994 and Wolfbeis et al, 1995. Rao does not teach the indentation having a second thickness that is less than the first thickness and a membrane having a first thickness over the at least one aperture and having a second thickness over the second and third apertures. Olivier teaches a well plate having an indentation having a second thickness that is greater than the first thickness (Figure 7). Olivier also teaches a membrane that covers the third aperture at the bottom of the well. The thickness of one sensor has been found to be 0.5 mm (Rao et al1994, p. 1141) the thickness of a second sensor has been made to be 2-4 μm (Wolfbeis et al 1995, p. 136). Both sensors sit upon apertures of the bottom of the well. Heat-sealing the membrane on the bottom of the well causes the filter material to soften or melt and fuse together forming an integral fluid tight seal ([0021]). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Rao with Olivier because the design of the well plate in Olivier would allow for the membrane to be on the bottom of the well to be used to separate the fluid from the solid material after a reaction had been completed.

Response to Arguments

1. Applicant's arguments filed 08/30/2007 have been fully considered but they are not persuasive. The following reasons are why:

2. Regarding Claims 1 and 19, applicant attempts to explain that the "opening" and the "aperture through the at least one surface of the well" are two separate elements and that Rao does not disclose an aperture in the at least one surface of the well that is configured to provide a gas supply to the interior of the well and that an "aperture" is distinct from the "opening of the well." Examiner respectfully disagrees. Examiner, by giving Claim 1 and 19 their broadest reasonable interpretation (as shown in the original claims and the amended claims, does not specifically state that the aperture and the opening of the well can not be the same or on the same surface of the well. Furthermore, Rao teaches in Figure 2, two apertures for air to be supplied to the interior of the well. Air is shown to be supplied in one direction, but can also be reversed. The output air supply as shown can be considered to either be part of the top surface or even attached to the far side wall of the well. Although applicant has tried to give a valid reason as to why the "opening" of the well and the "aperture" of the well are distinct, it is not pertinent in this case, because Claims 1 and 19 are deficient in specifically stating the "opening" and the "aperture" are distinct from each other.

3. Regarding Applicant's argument that neither Olivier nor Rao teach or suggest providing a gas supply access to the interior of the well through an aperture through a surface of the well (See Examiner's response above).

4. Regarding Claims 2 and 21, applicant argues that neither Rao nor Olivier teaches "the at least one aperture is through the bottom surface" of each well. Examiner respectfully disagrees. Examiner takes the position that Olivier does indeed teach that there is an "aperture through the bottom surface of the well (Figures 6-8 Item number 33)." This aperture although it is used as a drain, can also be used for a gas supply into the well. Examiner would also like to point out that applicant in remarks admits on the record that this aperture is usually filtrate (not limited to just filtrate). Olivier does not state that this direction of flow is unidirectional, therefore given its broadest interpretation, the direction of flow is two way, which means that this aperture can indeed be used for a gas supply.

5. Regarding Claims 7 & 29, applicant argues that Rao does not teach or suggest a gas permeable membrane that covers an aperture in a surface of the well that is used to provide a gas supply to the interior of the well. Examiner respectfully disagrees. Examiner, by giving the original and amended Claim 7 its most broad reasonable interpretation, is anticipated by Rao. Claim 7 "further comprises at least one membrane" (does not state there is only one membrane) coupled to at least one surface of each well ([0097]) and covering the at least one aperture (aperture can be defined as an opening of the well, but also a window for exposing the chemical sensor to the excitation light), wherein the membrane is formed from a gas permeable membrane and the gas is supplied through the membrane. Examiner takes the position that the claim as written, anticipates a chemical sensor comprising a polymeric membrane, as taught by Rao ([0096]). Examiner also takes the position that if fluid can penetrate this

polymeric membrane, so can a gas, therefore the gas is also supplied through the membrane to the inside of the well as it migrates through the membrane and towards the aperture and closer to the inside of the well. Examiner gratefully appreciates that applicant has pointed out that [0057] may refer to Figure 8, but Examiner would like to specifically point out that Rao teaches this as an example (note: "i.e.") and takes the position that it is not limited to Figure 8. Figure 2 also shows the gas supply as claimed, and can also be used with the ACRO 50 0.2 μm PTFE filter.

6. Regarding Claims 15-17, 21, 24, and 31, applicant argues that Olivier does not disclose an aperture in a surface of the well that is configured to provide a gas supply access to the interior of the well. Examiner respectfully disagrees. Olivier teaches a drain (Examiner takes the position that a drain defines a gas supply access) that can be configured to supply gas to the interior of the well. In Olivier's case, Olivier uses the Item number 33 as a drain (See above explanation).

7. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Rao teaches that in small volumes, probes compete with cells for oxygen, which distorts the result from the bioprocess [0009]. Examiner takes the position that motivation also comes from the

fact that cells die without a proper oxygen supply, in a small volume, where cells are in a dense state; supplying gas through the bottom of the well as in the drain in Olivier would be something one or ordinary skill in the art would understand to benefit cell culture growing in small volumes and as a result would be motivated to combine the two references.

8. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bobby Ramdhanie, Ph.D. whose telephone number is 571-270-3240. The examiner can normally be reached on Mon-Fri 8-5 (Alt Fri off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on 571-272-1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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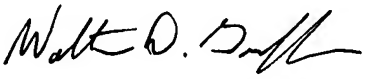

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